WEST Search History

DATE: Friday, August 29, 2003

Set Name side by side	Query	Hit Count	Set Name result set
DB=USPT,PGPB,JPAB,EPAB,DWPI; THES=ASSIGNEE; PLUR=YES; OP=ADJ			
L8	HAVRIX	22	L8
L7	HAV adj vaccine and Smithkline adj beacham	0	L7
L6	HAVRIX and Smithkline adj beacham	0	L6
L5	HAVRIX1440	0	L5
L4	MERCK and HAV adj vaccine	12	L4
L3	VAQTA and merck	1	L3
DB=USPT,PGPB,JPAB,EPAB,DWPI; PLUR=YES; OP=ADJ			
L2	"MERCK" and VAQTA	1	L2
L1	'MERCK'!	60630	L1

END OF SEARCH HISTORY

NCBI PubMed National Library of Medicine NLM

PubMed Nucleotide Protein Genome Structure PMC Taxonomy OMIM Books

Search PubMed for HAV purification and S.G.trypsin Preview Go

Clear

Limits Preview/Index History Clipboard Details

- Search History will be lost after eight hours of inactivity.
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- Search numbers may not be continuous; all searches are represented.

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Related Resources

Search	Most Recent Queries	Time	Result
#28	Search **HAV purification and S.G.trypsin** Limits: **Publication Date to 2001/12/10**	07:41:38	313
#25	Search **HAV purification by S.G.trypsin** Limits: **Publication Date to 2001/12/10**	07:40:41	313
#23	Search **virus purification by S.G.trypsin** Limits: **Publication Date to 2001/12/10**	07:39:05	83043
#22	Search **S.G.trypsin and virus purification** Limits: **Publication Date to 2001/12/10**	07:37:49	83043
#21	Search **S.G. trypsin and virus purification** Limits: **Publication Date to 2001/12/10**	07:37:43	0
#20	Search **Streptomyces griseus trypsin and virus purification** Limits: **Publication Date to 2001/12/10**	07:37:31	0
#15	Search **pronase and virus purification** Limits: **Publication Date to 2001/12/10**	07:36:27	105
#17	**Related Articles** for **PubMed** (Select **2066385**)	07:34:31	109
#14	Search **pronase and protein purification** Limits: **Publication Date to 2001/12/10**	07:32:11	986
#10	Search **pronase and vaccine preparation** Limits: **Publication Date to 2001/12/10**	07:30:16	4
#9	Search **pronase and antigen preparation** Limits: **Publication Date to 2001/12/10**	07:29:50	57
#5	Search **pronase and virus preparation** Field: **All Fields,** Limits: **Publication Date to 2001/12/10**	07:26:41	6
#4	Search **pronase and virus preparation**	07:26:16	6
#3	Search **S.g. trypsin and virus preparation**	07:25:35	0
#2	Search **S.g. trypsin and antigen preparation**	07:25:28	0
#1	Search **S.g. trypsin and vaccine preparation**	07:25:17	0

Clear History

Write to the Help Desk

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show files
File 155:MEDLINE(R) 1966-2003/Jul W2
         (c) format only 2003 The Dialog Corp.
File   5:Biosis Previews(R) 1969-2003/Jul W2
         (c) 2003 BIOSIS
File  34:SciSearch(R) Cited Ref Sci 1990-2003/Jul W2
         (c) 2003 Inst for Sci Info
File  35:Dissertation Abs Online 1861-2003/Jun
         (c) 2003 ProQuest Info&Learning
File  71:ELSEVIER BIOBASE 1994-2003/Jul W2
         (c) 2003  Elsevier Science B.V.
File  73:EMBASE 1974-2003/Jul W2
         (c) 2003 Elsevier Science B.V.
File  94:JICST-EPlus 1985-2003/Jul W1
         (c)2003 Japan Science and Tech Corp(JST)
File 144:Pascal 1973-2003/Jul W1
         (c) 2003 INIST/CNRS
File 340:CLAIMS(R)/US Patent 1950-03/Jul 17
         (c) 2003 IFI/CLAIMS(R)
File 345:Inpadoc/Fam.& Legal Stat 1968-2003/UD=200328
         (c) 2003 EPO
File 351:Derwent WPI 1963-2003/UD,UM &UP=200345
         (c) 2003  Thomson Derwent
File 357:Derwent Biotech Res. _1982-2003/Jul W3
         (c) 2003 Thomson Derwent & ISI
File 434:SciSearch(R) Cited Ref Sci 1974-1989/Dec
         (c) 1998 Inst for Sci Info
File 440:Current Contents Search(R) 1990-2003/Jul 17
         (c) 2003 Inst for Sci Info
?set hilight on
HILIGHT set on as ' '
?ds

Set     Items   Description
S1       4310   (HEPATITIS(W)A OR HAV) AND (NUCLEIC(W)ACID(W)DEGRADING(W)A-
            GENT OR ENZYME? OR DNASE)
S2       2522   RD (unique items)
S3          3   S2 AND (MICROBIAL(W)PROTEASE OR PRONASE)
?t3/3 ab/1-3
>>>No matching display code(s) found in file(s): 345

 3/AB/1     (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2003 The Dialog Corp. All rts. reserv.

14236221   22147529   PMID: 12153026
  Contribution of microbial activity to virus reduction in saturated soil.
  Nasser A M; Glozman R; Nitzan Y; et al
  Water Quality Research Laboratory, National Public Health Laboratories,
Ministry of Health, Tel-Aviv, Israel. abid.nasser@phlta.health.gov.il
  Water research (England)  May 2002,  36 (10)  p2589-95,  ISSN 0043-1354
Journal Code: 0105072
  Document type: Journal Article
  Languages: ENGLISH
  Main Citation Owner: NLM
  Record type: Completed
  Application of wastewater to soil may result in the contamination of
groundwater and soil with pathogenic microorganisms and other biological
and chemical agents. This study was performed to determine the antiviral
microbial activity of soil saturated with secondary effluent. Low
concentrations (0.05mg/ml) of protease pronase resulted in the
inactivation of more than 90% of seeded Cox-A9 virus, whereas Poliovirus
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type 1, Hepatitis A virus (HAV) and MS2 bacteriophages were found to be insensitive to the enzyme activity. Exposure of Cox A9 virus to P. aeruginosa extracellular enzymes resulted in 99% inactivation of the seeded virus. Hepatitis A virus was found to be as sensitive as the Cox A9 virus, whereas Poliovirus 1 and MS2 were found to be insensitive to P. aeruginosa extracellular enzymatic activity. Furthermore, the time required for 99% reduction (T99) of Cox A9 and MS-2 Bacteriophage, at 15 degrees C, in soil saturated with secondary effluent was found to be 7 and 21 days, respectively. Faster inactivation was observed for MS2 and Cox A9 in soil saturated with secondary effluent incubated at 30 degrees C, T99 of 2 and 0.3 days, respectively. Although the concentration of the total bacterial count in the soil samples increased from 10(3) cfu/g to 10(5) cfu/g after 20 days of incubation at 30 degrees C, the proteolytic activity was below the detection level. The results of this study indicate that the virucidal effect of microbial activity is virus type dependent. Furthermore microbial activity in the soil material can be enhanced by the application of secondary effluent at higher temperature. The results also showed that MS2 bacteriophage can be used to predict viral contamination of soil and groundwater.

3/AB/2 (Item 1 from file: 340)
DIALOG(R)File 340:CLAIMS(R)/US Patent
(c) 2003 IFI/CLAIMS(R). All rts. reserv.

Dialog Acc No: 10380092 IFI Acc No: 2003-0124511 IFI Acc No: 2003-0035643
Document Type: C
METHOD OF PRODUCTION OF PURIFIED HEPATITIS A VIRUS PARTICLES AND VACCINE PREPARATION
Inventors: Barrett Noel (AT); Meyer Heidi (AT); Mitterer Artur (AT); Tauer Christa (AT)
Assignee: Unassigned Or Assigned To Individual
Assignee Code: 68000
Publication (No,Date), Applic (No,Date):
US 20030124511 20030703 US 20016205 20011210
Publication Kind: A1
Priority Applic(No,Date): US 20016205 20011210

Abstract: The present invention provides methods of purification of Hepatitis A Virus from the supernatant of an infected cell culture and production of a preparation of purified HAV antigen. The present invention is also directed to an HAV vaccine composition comprising a preparation consisting of purified mature HAV particles in an amount sufficient to induce a protective immune response in a mammal.

3/AB/3 (Item 2 from file: 340)
DIALOG(R)File 340:CLAIMS(R)/US Patent
(c) 2003 IFI/CLAIMS(R). All rts. reserv.

Dialog Acc No: 10364444 IFI Acc No: 2003-0108861 IFI Acc No: 2003-0030897
Document Type: C
METHOD OF LARGE SCALE PRODUCTION OF HEPATITIS A VIRUS
Inventors: Barrett Noel (AT); Dorner Friedrich (AT); Meyer Heidi (AT); Mundt Wolfgang (AT); Reiter Manfred (AT)
Assignee: Unassigned Or Assigned To Individual
Assignee Code: 68000
Publication (No,Date), Applic (No,Date):
US 20030108861 20030612 US 20016882 20011210
Publication Kind: A1
Priority Applic(No,Date): US 20016882 20011210

Abstract: The present invention provides methods of large scale production of Hepatitis A Virus (HAV) on VERO cells bound to microcarrier. The invention also provides for methods of isolation of HAV from the cell culture supernatant of HAV infected VERO cells.
?ds

Set	Items	Description
S1	4310	(HEPATITIS(W)A OR HAV) AND (NUCLEIC(W)ACID(W)DEGRADING(W)AGENT OR ENZYME? OR DNASE)
S2	2522	RD (unique items)
S3	3	S2 AND (MICROBIAL(W)PROTEASE OR PRONASE)
S4	457	S2 AND (PREP? OR PRODUCT? OR PROCESS? OR MANUF?)
S5	149	S4 (S)VACCIN?
S6	12	S5 (S)PARTICL?
S7	11	S6 NOT S3

?t7/3 ab/1-11
>>>No matching display code(s) found in file(s): 345

7/AB/1 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2003 The Dialog Corp. All rts. reserv.

11971610 99416401 PMID: 10486933
Development of DNA vaccines for foot-and-mouth disease, evaluation of vaccines encoding replicating and non-replicating nucleic acids in swine.
Beard C; Ward G; Rieder E; Chinsangaram J; Grubman M J; Mason P W
Plum Island Animal Disease Center, Agricultural Research Service, United States Department of Agriculture, Greenport, NY 11944-0848, USA.
Journal of biotechnology (NETHERLANDS) Aug 20 1999, 73 (2-3) p243-9, ISSN 0168-1656 Journal Code: 8411927
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
We have developed naked DNA vaccine candidates for foot-and-mouth disease (FMD), an important disease of domestic animals. The virus that causes this disease, FMDV, is a member of the picornavirus family, which includes many important human pathogens, such as poliovirus, hepatitis A virus, and rhinovirus. Picornaviruses are characterized by a small (7-9000 nucleotide) RNA genome that encodes capsid proteins, processing proteinases, and enzymes required for RNA replication. We have developed two different types of DNA vaccines for FMD. The first DNA vaccine , pP12X3C, encodes the viral capsid gene (P1) and the processing proteinase (3C). Cells transfected with this DNA produce processed viral antigen, and animals inoculated with this DNA using a gene gun produced detectable antiviral immune responses. Mouse inoculations with this plasmid, and with a derivative containing a mutation in the 3C proteinase, indicated that capsid assembly was essential for induction of neutralizing antibody responses. The second DNA vaccine candidate, pWRMHX, encodes the entire FMDV genome, including the RNA-dependent RNA polymerase, permitting the plasmid-encoded viral genomes to undergo amplification in susceptible cells. pWRMHX encodes a mutation at the cell binding site, preventing the replicated genomes from causing disease. Swine inoculated with this vaccine candidate produce viral particles lacking the cell binding site, and neutralizing antibodies that recognize the virus. Comparison of the immune responses elicited by pP12X3C and pWRMHX in swine indicate that the plasmid encoding the replicating genome stimulated a stronger immune response, and swine inoculated with pWRMHX by the intramuscular, intradermal, or gene gun routes were partially protected from a highly virulent FMD challenge.

7/AB/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2003 The Dialog Corp. All rts. reserv.

11430453 98312973 PMID: 9650953
Recombinant hepatitis A virus antigen: improved production and utility in diagnostic immunoassays.
LaBrecque F D; LaBrecque D R; Klinzman D; Perlman S; Cederna J B; Winokur P L; Han J Q; Stapleton J T
Department of Internal Medicine, Iowa City Veterans Affairs Medical Center and The University of Iowa, 52242, USA.
Journal of clinical microbiology (UNITED STATES) Jul 1998, 36 (7) p2014-8, ISSN 0095-1137 Journal Code: 7505564
Contract/Grant No.: RR0059; RR; NCRR
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Hepatitis A virus (HAV) immunoassays use cell culture-derived HAV antigen to detect HAV -specific antibodies. The current method of production of HAV antigen in tissue culture is time-consuming and expensive. We previously expressed the HAV open reading frame in recombinant vaccinia viruses (rV-ORF). The recombinant HAV polyprotein was accurately processed and was assembled into subviral particles . These particles were bound by HAV -neutralizing antibodies and were able to elicit antibodies which were detected by commercial immunoassays. The present investigation compared the production of HAV antigen by standard tissue culture methods to the production of HAV antigen with the recombinant vaccinia virus system. In addition, HAV and rV-ORF antigens were assessed for their utility in diagnostic immunoassays. Serum or plasma samples from HAV antibody-positive and antibody-negative individuals were evaluated by immunoassay that used either HAV or rV-ORF antigen. All samples (86 of 86) in which HAV antibody was detected by a commercial enzyme -linked immunosorbent assay (ELISA) also tested positive by the recombinant antigen-based immunoassay (VacRIA). Similarly, all samples (50 of 50) that were HAV antibody negative also tested negative by the VacRIA. The lower limit of detection of HAV antibody was similar among immunoassays with either HAV or rV-ORF antigen. Thus, in the population studied, the sensitivity and specificity of the VacRIA were equivalent to those of the commercial ELISA. Since production of recombinant antigen is faster and less expensive than production of traditional HAV antigen, the development of diagnostic HAV antibody tests with recombinant HAV antigen appears warranted.

7/AB/3 (Item 1 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2003 Inst for Sci Info. All rts. reserv.

07840527 Genuine Article#: 214FJ Number of References: 15
Title: Evaluation of the purity of a purified, inactivated hepatitis A vaccine (VAQTA(TM)) (ABSTRACT AVAILABLE)
Author(s): Hennessey JP (REPRINT) ; Oswald CB; Dong ZY; Lewis JA; Sitrin RD
Corporate Source: MERCK RES LABS,BIOPROC & BIOANALYT RES, POB 4/W POINT//PA/19486 (REPRINT)
Journal: VACCINE, 1999, V17, N22 (JUL 16), P2830-2835
ISSN: 0264-410X Publication date: 19990716
Publisher: ELSEVIER SCI LTD, THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD OX5 1GB, OXON, ENGLAND
Language: English Document Type: ARTICLE
Abstract: Manufacture of VAQTA(TM), an inactivated hepatitis A virus vaccine , includes extensive purification of the intact virus particle

to remove endogenous components from the host cell culture lysate as well as compounds introduced in the upstream purification process . Analysis of the final purified hepatitis A virus product by SDS-PAGE prior to inactivation shows that greater than 95% of the protein in the preparation is found in four protein bands, which have been confirmed to be hepatitis A virus capsid proteins VP0. VP1, VP2 and VP3 based on Western blot and mass spectrometry analyses. Validation of the manufacturing process and direct analysis of the final product were used to demonstrate that no other specific host cell-derived components are detected and that process residuals are all below the limits of detection of the assays used. Establishment of a rigorous standard of high purity for this product was pursued to minimize the impact of impurities during clinical development of this product and will facilitate the incorporation of this product into combination vaccines . (C) 1999 Elsevier Science Ltd. All rights reserved.

7/AB/4 (Item 2 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2003 Inst for Sci Info. All rts. reserv.

03674999 Genuine Article#: PW815 Number of References: 66
Title: VIRAL-RNA MODULATES THE ACID SENSITIVITY OF FOOT-AND-MOUTH-DISEASE VIRUS CAPSIDS (Abstract Available)
Author(s): CURRY S; ABRAMS CC; FRY E; CROWTHER JC; BELSHAM GJ; STUART DI; KING AMQ
Corporate Source: INST ANIM HLTH,PIRBRIGHT LAB/SURREY GU24 0NF//ENGLAND/; INST ANIM HLTH,PIRBRIGHT LAB/SURREY GU24 0NF//ENGLAND/; UNIV OXFORD,MOLEC BIOPHYS LAB/OXFORD OX1 3QU//ENGLAND/; OXFORD CTR MOLEC SCI,NEW CHEM LAB/OXFORD OX1 3QT//ENGLAND/
Journal: JOURNAL OF VIROLOGY, 1995, V69, N1 (JAN), P430-438
ISSN: 0022-538X
Language: ENGLISH Document Type: ARTICLE
Abstract: Foot-and-mouth disease virus (FMDV) manifests an extreme sensitivity to acid, which is thought to be important for entry of the RNA genome into the cell. We have compared the low-pH-induced disassembly in vitro of virions and natural empty capsids of three subtypes of serotype A FMDV by enzyme -linked immunosorbent assay and sucrose gradient sedimentation analysis. For all three subtypes (A22 Iraq 24/64, A10(61), and A24 Cruzeiro), the empty capsid was more stable by 0.5 pH unit on average than the corresponding virion. Unexpectedly, in the natural empty capsids used in this study, the precursor capsid protein VP0 was found largely to be cleaved into VP2 and VP4. For picornaviruses the processing of VP0 is closely associated with encapsidation of viral RNA, which is considered likely to play a catalytic role in the cleavage. Investigation of the cleavage of WO in natural empty capsids failed to implicate the viral RNA. However, it remains possible that these particles arise from abortive attempts to encapsidate RNA. Empty capsids expressed from a vaccinia virus recombinant showed essentially the same acid lability as natural empty capsids, despite differing considerably in the extent of VP0 processing , with the synthetic particles containing almost exclusively uncleaved VP0. These results indicate that it is the viral RNA that modulates acid lability in FMDV. In all cases the capsids dissociate at low pH directly into pentameric subunits. Comparison of the three viruses indicates that FMDV A22 Iraq is about 0.5 pH unit more sensitive to low pH than types A10(61) and A24 Cruzeiro. Sequence analysis of the three subtypes identified several differences at the interface between pentamers and highlighted a His-cu-helix dipole interaction which spans the pentamer interface and appears likely to influence the acid lability of the virus.

7/AB/5 (Item 1 from file: 351)
DIALOG(R)File 351:Derwent WPI
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014396474
WPI Acc No: 2002-217177/200227
XRAM Acc No: C02-066479
Producing hepatitis B antigen suitable for use in vaccine for treatment and prophylaxis of hepatitis B virus infections, comprises purification of antigen in presence of reducing agent having free-thio group
Patent Assignee: SMITHKLINE BEECHAM BIOLOGICALS (SMIK); GLAXOSMITHKLINE BIOLOGICALS SA (GLAX)
Inventor: DE HEYDER K; SCHU P; SERANTONI M; VAN OPSTEL O; VAN OPSTAL O
Number of Countries: 097 Number of Patents: 004
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week
WO 200212287	A1	20020214	WO 2001EP9100	A	20010807	200227 B
AU 200182073	A	20020218	AU 200182073	A	20010807	200244
EP 1307473	A1	20030507	EP 2001960630	A	20010807	200332
			WO 2001EP9100	A	20010807	
NO 200300635	A	20030401	WO 2001EP9100	A	20010807	200336
			NO 2003635	A	20030207	

Priority Applications (No Type Date): GB 20011334 A 20010118; GB 200019728 A 20000810
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
WO 200212287	A1	E	37	C07K-014/02	

Designated States (National): AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
Designated States (Regional): AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW

AU 200182073	A		C07K-014/02	Based on patent WO 200212287
EP 1307473	A1	E	C07K-014/02	Based on patent WO 200212287

Designated States (Regional): AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR

NO 200300635	A		C07K-000/00	

Abstract (Basic): WO 200212287 A1
Abstract (Basic):

NOVELTY - Producing (M) a hepatitis B antigen suitable for use in a vaccine, comprising purification of the antigen in the presence of a reducing agent having free-SH group, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) an immunogenic hepatitis B antigen (I) obtained by (M); and

(2) a vaccine composition (II) comprising (I).

ACTIVITY - Hepatotropic; virucide; antiinflammatory.

MECHANISM OF ACTION - Vaccine. No supporting data given.

USE - (M) is useful for producing hepatitis B antigen. (I) is useful for treatment and prophylaxis of hepatitis B infections, especially treatment or prophylaxis of chronic hepatitis B infections. (I) is also useful in the manufacture of a medicament for treating the above said diseases.

ADVANTAGE - (I) is a stable immunogenic antigen without trace of thiomersal. (I) comprises less than 0.25 microgram mercury/20 microgram protein. (I) has a mean enzyme linked immunosorbant assay (ELISA) protein ratio greater than 1.5 and an RF1 (undefined) content with at

least a 3-fold lower inhibitory concentration (IC50) value than that of the hepatitis B surface antigen manufactured in the presence of thiomersal (claimed). The three bulk antigen preparations HEF001, HEF002 and HEF003, were tested for their reactivity with RF1 monoclonal antibody by enzyme linked immunosorbant assay (ELISA) inhibition assay. Ascitic fluid diluted at 1/50000 in saturation buffer was mixed 1:1 with various dilutions in phosphate buffered saline (PBS) of the HBsAg samples to be tested. Mixtures were incubated for 1 hour at 37 degrees C before being transferred for 1 hour at 37 degrees C onto plates coated with a standard preparation of hepatitis B bulk antigen (HBsAg) (a lot of bulk antigen (Hep 186) purified by thiomersal process). After washing, biotin-conjugated sheep anti-mouse immunoglobulin G (IgG) was added and incubated for 1 hour at 37 degrees C. The streptavidin-biotinylated peroxidase complex was added to the same wells and incubated for 30 minutes at 37 degrees C. Plates were washed and incubated with a solution of OPDA (undefined) 0.04%, H2O2 0.03% in 0.1 M citrate buffer pH 4.5 for 20 minutes at room temperature. The reaction was stopped and the optical densities were measured and plotted graphically. The results showed that 4-7 fold less HEF antigen is required to inhibit RF1 binding. This showed that antigen prepared by the modified process has an increased presentation of the RF1 epitope compared to HEP bulk antigen.

pp; 37 DwgNo 0/3

7/AB/6 (Item 2 from file: 351)
DIALOG(R)File 351:Derwent WPI
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014277521
WPI Acc No: 2002-098223/200213
XRAM Acc No: C02-030677

New proteins comprising a modified hepatitis B core antigen, useful as a vaccine in prophylactic or therapeutic vaccination of the human or animal body, particularly against hepatitis B virus infection

Patent Assignee: CELLTECH PHARM LTD (CELL-N)
Inventor: BORISOVA G; LI J; PAGE M; PUMPENS P
Number of Countries: 097 Number of Patents: 003
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
WO 200198333	A2	20011227	WO 2001GB2817	A	20010622	200213	B
AU 200166163	A	20020102	AU 200166163	A	20010622	200230	
EP 1294893	A2	20030326	EP 2001943625	A	20010622	200323	
			WO 2001GB2817	A	20010622		

Priority Applications (No Type Date): GB 200024544 A 20001006; GB 200015308 A 20000622
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
WO 200198333	A2	E	39	C07K-014/005	

Designated States (National): AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
Designated States (Regional): AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW

AU 200166163	A		C07K-014/005	Based on patent WO 200198333
EP 1294893	A2	E	C12N-015/51	Based on patent WO 200198333

Designated States (Regional): AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR

Abstract (Basic): WO 200198333 A2

Abstract (Basic):

NOVELTY - A protein comprising hepatitis B core antigen (HBcAg), where one or more of the four arginine repeats is absent and a C-terminal cysteine residue is present, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a particle comprising multiple copies of the novel protein;

(2) a nucleic acid molecule encoding the novel protein;

(3) a host cell transformed or transfected with the nucleic acid of (2);

(4) producing the novel protein by culturing the cell of (30 under expression conditions, and recovering the polypeptide;

(5) a pharmaceutical composition comprising the protein, the particle or the nucleic acid molecule, and a pharmaceutical carrier or diluent; and

(6) vaccination or therapy of a subject comprising administering to the subject the protein, particle or nucleic acid molecule.

ACTIVITY - Antiviral; antibacterial; antiprotozoal.

No biological data is given.

MECHANISM OF ACTION - Vaccine; gene therapy.

USE - The protein, particle or nucleic acid molecule is useful as a vaccine or in a method of prophylactic or therapeutic vaccination of the human or animal body, particularly against HBV. The protein, particle or nucleic acid molecule is also useful for the manufacture of a medicament for prophylactic or therapeutic vaccination of the human or animal body against HBV. (All claimed). The nucleic acid encoding the protein may be used in gene therapy or DNA vaccination protocols. The protein, particle or nucleic acid may also be used as the basis of a prophylactic vaccine against a range of diseases, e.g. HBV, hepatitis A virus (HAV), hepatitis C virus (HCV), influenza, foot-and-mouth disease, polio, herpes, rabies, acquired immunodeficiency syndrome (AIDS), dengue fever, yellow fever, malaria, tuberculosis, whooping cough, salmonellosis, typhoid, food poisoning, diarrhea, meningitis or gonorrhea.

pp; 39 DwgNo 0/8

7/AB/7 (Item 1 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.
(c) 2003 Thomson Derwent & ISI. All rts. reserv.

0289310 DBR Accession No.: 2002-11157 PATENT
Producing hepatitis B antigen suitable for use in vaccine for treatment and prophylaxis of hepatitis B virus infections, comprises purification of antigen in presence of reducing agent having free-thio group - recombinant vaccine useful for virus infection and bacterium infection therapy
AUTHOR: DE HEYDER K; SCHU P; SERANTONI M; VAN OPSTEL O
PATENT ASSIGNEE: SMITHKLINE BEECHAM BIOLOGICALS 2002
PATENT NUMBER: WO 200212287 PATENT DATE: 20020214 WPI ACCESSION NO.: 2002-217177 (200227)
PRIORITY APPLIC. NO.: GB 20011334 APPLIC. DATE: 20010118
NATIONAL APPLIC. NO.: WO 2001EP9100 APPLIC. DATE: 20010807
LANGUAGE: English
ABSTRACT: DERWENT ABSTRACT: NOVELTY - Producing (M) a hepatitis B antigen suitable for use in a vaccine , comprising purification of the antigen in the presence of a reducing agent having free-SH group, is new. DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) an immunogenic hepatitis B antigen (I) obtained by (M); and (2) a vaccine composition (II) comprising (I). BIOTECHNOLOGY - Preferred Method: A crude form of (I) is prepared by subjecting (I) to gel permeation chromatography and ion-exchange chromatography, and

mixing with a reducing agent having a free SH-group e.g. cysteine, glutathione, dithiothreitol or beta-mercaptoethanol. Cysteine is added to a final concentration of 1-10 mM, preferably 2 mM. (I) is purified in the presence of thiomersal before treating with the reducing agent. (I) is at least as immunogenic and antigenic as a hepatitis B antigen manufactured in the presence of thiomersal. Preferred Composition: (II) comprises a TH-1 inducing adjuvant e.g. 3-de-O-acylated monophosphoryl lipid a (3-DMPL), QS21 (saponin), 3-DMPL and QS21, or CpG oligonucleotide, and one or more antigens selected from diphtheria toxoid (D), tetanus toxoid (T), acellular pertussis antigens (Pa), inactivated polio virus (IPV), Hemophilus influenzae antigen (Hib), hepatitis A antigen, herpes simplex virus (HSV), Chlamydia, GSB (undefined), human papilloma virus (HPV), Streptococcus pneumoniae and neisseria antigens. (I) is a surface antigen. (II) optionally comprises a cysteine solution. ACTIVITY - Hepatotropic; virucide; antiinflammatory. MECHANISM OF ACTION - Vaccine . No supporting data given. USE - (M) is useful for producing hepatitis B antigen. (I) is useful for treatment and prophylaxis of hepatitis B infections, especially treatment or prophylaxis of chronic hepatitis B infections. (I) is also useful in the manufacture of a medicament for treating the above said diseases. ADVANTAGE - (I) is a stable immunogenic antigen without trace of thiomersal. (I) comprises less than 0.25 microgram mercury/20 microgram protein. (I) has a mean enzyme linked immunosorbant assay (ELISA) protein ratio greater than 1.5 and an RF1 (undefined) content with at least a 3-fold lower inhibitory concentration (IC50) value than that of the hepatitis B surface antigen manufactured in the presence of thiomersal (claimed). The three bulk antigen preparations HEF001, HEF002 and HEF003, were tested for their reactivity with RF1 monoclonal antibody by enzyme linked immunosorbant assay (ELISA) inhibition assay. Ascitic fluid diluted at 1/50000 in saturation buffer was mixed 1:1 with various dilutions in phosphate buffered saline (PBS) of the HBsAg samples to be tested. Mixtures were incubated for 1 hour at 37 degrees C before being transferred for 1 hour at 37 degrees C onto plates coated with a standard preparation of hepatitis B bulk antigen (HBsAg) (a lot of bulk antigen (Hep 186) purified by thiomersal process). After washing, biotin-conjugated sheep anti-mouse immunoglobulin G (IgG) was added and incubated for 1 hour at 37 degrees C. The streptavidin-biotinylated peroxidase complex was added to the same wells and incubated for 30 minutes at 37 degrees C. Plates were washed and incubated with a solution of OPDA (undefined) 0.04%, H2O2 0.03% in 0.1 M citrate buffer pH 4.5 for 20 minutes at room temperature. The reaction was stopped and the optical densities were measured and plotted graphically. The results showed that 4-7 fold less HEF antigen is required to inhibit RF1 binding. This showed that antigen prepared by the modified process has an increased presentation of the RF1 epitope compared to HEP bulk antigen. EXAMPLE - Hepatitis B surface antigen (HBsAg) of SB Biologicals hepatitis B monovalent vaccine was expressed as a recombinant protein in Saccharomyces cerevisiae. The 24 kD protein was produced intracellularly and accumulated in the recombinant yeast cells. The yeast cells were harvested and disrupted to liberate the desired protein. Subsequently, the cell homogenate, containing the soluble surface antigen particles , was prepurified in a series of precipitations and then concentrated by ultrafiltration. Further purification of the recombinant antigen was performed in subsequent chromatographic separations. In the first step, the crude antigen concentrate was subjected to gel permeation chromatography on Sepharose 4B medium. Thiomersal was present in the elution buffer at 4B gel permeation chromatography. The elution buffer had 10 mM Tris, 5% ethylene glycol, pH 7.0, 50 mg/l thiomersal. Most of the thiomersal was removed during the subsequent purification steps including ion exchange chromatography, ultracentrifugation and desalting, so that purified

bulk antigen preparations prepared by the original process contained 1.2-2 microgram of thiomersal for 20 microgram of protein. Ion-Exchange chromatography was performed using a DEAE (undefined)-matrix and the pool was then subjected to a Cesium-gradient ultracentrifugation on 4 pre-established layers of different Cesium chloride concentrations. The antigen particles were separated, and Cesium chloride was removed. In the thiomersal free process , thiomersal was not included in the elution buffer at the 4B gel permeation chromatography, and Cysteine was added to the eluate pool from the anion exchange chromatography. It was found that omission of thiomersal from the 4B gel permeation buffer results in precipitation of hepatitis B surface antigen (HBsAg) particles during the CsCl density gradient centrifugation step with loss of product and aggregation or clumping of the recovered antigen. Addition of cysteine at 2 mM final concentration to the eluate pool from the preceding anion exchange chromatography step prevented precipitation and loss of antigen during CsCl density centrifugation. Cysteine was preferred for the treatment as it is a naturally occurring amino acid and can be removed at the subsequent desalting step on a gel permeation column using Sepharose 4BCLFF as column matrix. The thiomersal free process yielded three lots of bulk antigens identified as HEF001, HEF002 and HEF003, of purity and properties comparable to antigen from the process using thiomersal. (37 pages)

7/AB/8 (Item 2 from file: 357)
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0285924 DBR Accession No.: 2002-07771 PATENT
New proteins comprising a modified hepatitis B core antigen, useful as a vaccine in prophylactic or therapeutic vaccination of the human or animal body, particularly against hepatitis B virus infection - recombinant protein production via plasmid expression in host cell and virus core antigen useful for vaccine and in disease gene therapy
AUTHOR: PAGE M; LI J; PUMPENS P
PATENT ASSIGNEE: CELLTECH PHARM LTD 2001
PATENT NUMBER: WO 200198333 PATENT DATE: 20011227 WPI ACCESSION NO.: 2002-098223 (200213)
PRIORITY APPLIC. NO.: GB 200024544 APPLIC. DATE: 20001006
NATIONAL APPLIC. NO.: WO 2001GB2817 APPLIC. DATE: 20010622
LANGUAGE: English
ABSTRACT: DERWENT ABSTRACT: NOVELTY - A protein comprising hepatitis B core antigen (HBcAg), where one or more of the four arginine repeats is absent and a C-terminal cysteine residue is present, is new. DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) a particle comprising multiple copies of the novel protein; (2) a nucleic acid molecule encoding the novel protein; (3) a host cell transformed or transfected with the nucleic acid of (2); (4) producing the novel protein by culturing the cell of (30 under expression conditions, and recovering the polypeptide; (5) a pharmaceutical composition comprising the protein, the particle or the nucleic acid molecule, and a pharmaceutical carrier or diluent; and (6) vaccination or therapy of a subject comprising administering to the subject the protein, particle or nucleic acid molecule. BIOTECHNOLOGY - Preferred Protein: A first epitope from a protein other than HBcAg is present in place of the absent arginine repeats. The first arginine repeat is present and the second to fourth arginine repeats are absent. A sequence lying between residues 145-182 or 150-177 of HBcAg is absent. The protein further comprises a second epitope from a protein other than HBcAg, the second epitope being in the el loop. In particular, the second epitope is a B-cell epitope and the first epitope is a T-cell

epitope. Preferably, the first epitope is a T-helper cell epitope and the second epitope is a B-cell epitope. The protein may also comprise the first and second epitopes, where the epitopes are the same. The first and/or the second epitope are from hepatitis B virus (HBV), particularly from the pre-S1, pre-S2 or S region of HBV. The protein comprises the following elements linked in an N-terminal to C-terminal direction: (a) an N-terminal part of HBcAg, which mediates the formation of particles ; and (b) a C-terminal part of HBcAg comprising the C-terminal cysteine, where at least a part of the sequence of HBcAg from between the N-terminal part and the C-terminal part comprising one or more of the arginine repeats is absent. The protein also comprises the following elements linked in an N- to C-terminal direction: (a) an N-terminal part of HBcAg, which mediates the formation of particles ; (b) an epitope from a protein other than HBcAg; and (c) a C-terminal part of HBcAg comprising the C-terminal cysteine, where at least a part of the sequence of HBcAg between the N-terminal part and the C-terminal part comprising one or more of the arginine repeats is absent and is replaced by the epitope. The protein may also comprise the following elements linked in an N- to C-terminal direction: (a) an N-terminal part of the HBcAg sequence comprising residues 1-67; (b) an epitope from a protein other than HBcAg; (c) a second part of the HBcAg sequence comprising residues 91-144; and (d) a third part of the HBcAg sequence comprising the C-terminal cysteine, where at least a part of the sequence of HBcAg from between residue 145 and the C-terminal cysteine comprising one or more of the arginine repeats is absent. Alternatively, the protein may comprise the following elements linked in an N- to C-terminal direction: (a) an N-terminal part of the HBcAg sequence comprising residues 1-67; (b) an epitope from a protein other than HBcAg; (c) a second part of the HBcAg sequence comprising residues 91-144; (d) a further epitope from a protein other than HBcAg; and (e) a third part of the HBcAg sequence comprising the C-terminal cysteine, where at least a part of the sequence of HBcAg from between residues 145 and the C-terminal cysteine comprising one or more of the arginine repeats is absent. The nucleic acid molecule, which encodes the protein, is an expression vector. In particular, the sequence encoding one or more of the four arginine repeats of HBcAg is deleted and replaced with a restriction enzyme site unique to the nucleic acid molecule. ACTIVITY - Antiviral; antibacterial; antiprotozoal. No biological data is given. MECHANISM OF ACTION - Vaccine ; gene therapy. USE - The protein, particle or nucleic acid molecule is useful as a vaccine or in a method of prophylactic or therapeutic vaccination of the human or animal body, particularly against HBV. The protein, particle or nucleic acid molecule is also useful for the manufacture of a medicament for prophylactic or therapeutic vaccination of the human or animal body against HBV. (All claimed). The nucleic acid encoding the protein may be used in gene therapy or DNA vaccination protocols. The protein, particle or nucleic acid may also be used as the basis of a prophylactic vaccine against a range of diseases, e.g. HBV, hepatitis A virus (HAV), hepatitis C virus (HCV), influenza, foot-and-mouth disease, polio, herpes, rabies, acquired immunodeficiency syndrome (AIDS), dengue fever, yellow fever, malaria, tuberculosis, whooping cough, salmonellosis, typhoid, food poisoning, diarrhea, meningitis or gonorrhea. ADMINISTRATION - Administration may be parenteral, intramuscular, intravenous, intranasal, subcutaneous or transdermal administration. Dosage for the protein is 0.01-30, preferably 0.1-1 micro-g/kg. The dosage for the nucleic acid is 1 micro-g-10 mg, preferably from 100 micro-g-1 mg. The vaccine may be given in a single dose schedule or a multiple dose schedule. EXAMPLE - Full-length and C-terminally truncated hepatitis B core antigen (HBc) derivatives, which carried long foreign amino acid insertions at position 144, were constructed. HBV preS1, preS2, and human immunodeficiency virus (HIV)-1 Gag fragments of 50-100 amino

acids in length were used as such insertions, and the appropriate recombinant genes were expressed in Escherichia coli cells. The appropriate chimeric HBc and HBcDELTA derivatives were purified and examined antigenically and immunogenically. Subclass analysis of the induced anti-HBc immune response in mice showed that the immunoglobulin (Ig) ratio of IgG1, IgG2a and IgG2b antibodies was restored from the IgG1 greater than IgG2a at least IgG2b pattern. (39 pages)

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0241440 DBR Accession No.: 1999-11541
Development of DNA vaccines for foot-and-mouth-disease, evaluation of vaccines encoding replicating and non-replicating nucleic acids in pig - foot-and-mouth-disease virus-specific nucleic acid vaccine production and vector plasmid pP12X3C and plasmid pWRMHX-mediated gene transfer and expression in pig (conference paper)
AUTHOR: Beard C; Ward G; Rieder E; Chinsangaram J; Grubman M J; +Mason P W
CORPORATE AFFILIATE: USDA-ARS
CORPORATE SOURCE: Plum Island Animal Disease Center, North Atlantic Area, Agricultural Research Service, United Stated Department of Agriculture, P.O. Box 848, Greenport, NY 11944-0848, USA.
email:petermas@asrr.arsisda.gov
JOURNAL: J.Biotechnol. (73, 2-3, 243-49) 1999
ISSN: 0168-1656 CODEN: JBITD4
CONFERENCE PROCEEDINGS: New Approaches in Vaccine Development 1997, Australian Society of Biotechnology, Vienna, Austria, 1997.
LANGUAGE: English
ABSTRACT: Naked nucleic acid vaccine candidates for foot-and-mouth-disease (FMD), which is an important disease of many domestic animals, were developed. Foot-and-mouth-disease virus (FMDV), which causes this condition, is a member of the picorna virus family, which also includes many human pathogens such as polio virus, hepatitis A virus and rhino virus. A small (7-9,000 nucleotide) RNA genome, which encodes capsid proteins, processing proteases and the enzymes required for RNA replication are characteristic of picorna viruses. 2 Different types of nucleic acid vaccines were developed for use against FMD. Vector plasmid pP12X3C, which encoded the virus capsid gene (P1) and the processing protease (3C) and plasmid pWRMHX, which encoded the entire FMCV genome, were constructed and used as nucleic acid vaccines . Cells transfect with pP12X3C produced processed virus antigen and animals inoculated with it using a gene gun produced detectable anti virus immune responses. Pigs inoculated with pWRMHX produced virus particles which lacked the cell binding site and neutralizing antibodies that recognized the virus. The pigs were partially protected against FMDV challenge. (32 ref)

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0192480 DBR Accession No.: 96-02673 PATENT
Hepatitis G virus isolates, polypeptides and related nucleic acids - recombinant protein for disease therapy, recombinant vaccine, and DNA probe and DNA primer for disease diagnosis
AUTHOR: Kim J P; Fry K E; Young L M; Linnen J M; Wages J
CORPORATE SOURCE: Redwood City, CA, USA.
PATENT ASSIGNEE: Genelabs 1995

PATENT NUMBER: WO 9532291 PATENT DATE: 951130 WPI ACCESSION NO.: 96-049299 (9605)
PRIORITY APPLIC. NO.: US 389886 APPLIC. DATE: 950215
NATIONAL APPLIC. NO.: WO 95US6169 APPLIC. DATE: 950519
LANGUAGE: English
ABSTRACT: A non-A non-B non-C non-D non-E hepatitis virus, hepatitis G virus (HGV), protein (I) is claimed, where the HGV is transmissible in primates, is serologically distinct from hepatitis A virus, hepatitis B virus, hepatitis C virus, hepatitis D virus and hepatitis E virus, and is a member of the flaviviridae. (I) has an antigenic determinant specifically immunoreactive with HGV genomic DNA, cDNA or their complements containing an open reading frame with at least 40% homology to the disclosed protein sequences. Also claimed are: (I) fixed to a solid surface; synthetic (I); (I) prepared by genetic engineering; a (I) fusion protein with e.g. beta-galactosidase (EC-3.2.1.23), glutathione-transferase (EC-2.5.1.18) or particle -forming protein; fragments of (I); a cloning vector (phage lambda gt11) expressing HGV cDNA or DNA; a transformed cell (Escherichia coli) expressing (I); production of (I) by culturing the transformed cell; diagnostic kits and methods for HGV infection; a polynucleotide (DNA or cDNA) encoding (I) for use as a DNA probe or DNA primer in e.g. diagnosis; a (I)-containing vaccine ; and a (I)-specific monoclonal antibody and its production . (452pp)

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0131901 DBR Accession No.: 92-04393 PATENT
Purifying hepatitis A virus capsid - by ionexchange chromatography and gel filtration
PATENT ASSIGNEE: Merck-USA 1992
PATENT NUMBER: EP 468702 PATENT DATE: 920129 WPI ACCESSION NO.: 92-034427 (9205)
PRIORITY APPLIC. NO.: US 555020 APPLIC. DATE: 900718
NATIONAL APPLIC. NO.: EP 91306541 APPLIC. DATE: 910718
LANGUAGE: English
ABSTRACT: A method of purifying hepatitis A virus (HAV) capsids involves: (a) subjecting the aq. phase of a lysate of HAV infected cells to ionexchange chromatography; (b) subjecting the effluent of (a) to ionexchange chromatography; and (c) gel filtering the eluate of (b) containing HAV capsids. The product of this process is also claimed. The capsids obtained are free of contaminating 30 nm particles when observed by electron microscopy. Ionexchange chromatography steps (a) and (b) are preferably anion-exchange chromatography steps. Step (a) is preferably performed using 0.3-0.4 M NaCl, especially 0.35 M NaCl. Step (b) is preferably performed using 0.1-0.2 M (especially 0.15 M) NaCl for HAV capsid adsorption, and 0.3-0.4 M (especially 0.38 M) for HAV capsid elution. The method can be used to obtain extremely pure HAV capsids without the use of detergents or exogenous enzymes . The product can be used for vaccination against HAV infection. (8pp)
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